

AMENDMENTS TO THE CLAIMS

Please cancel Claims 1-10 without prejudice and insert therefore new Claims 11-18. This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-10 (canceled)

11. (new) A method for the treatment or prevention of a disease associated with deposition of A β in the brain comprising administering to a subject in need thereof a therapeutically effective amount of a growth hormone secretagogue or a pharmaceutically acceptable salt thereof and a therapeutically effective amount of a p38 kinase inhibitor or a pharmaceutically acceptable salt thereof.

12. (new) The method of Claim 11 wherein the disease is selected from Alzheimer's disease, age-related cognitive decline, mild cognitive impairment, cerebral amyloid angiopathy, multi-infarct dementia, dementia pugilistica and Down syndrome.

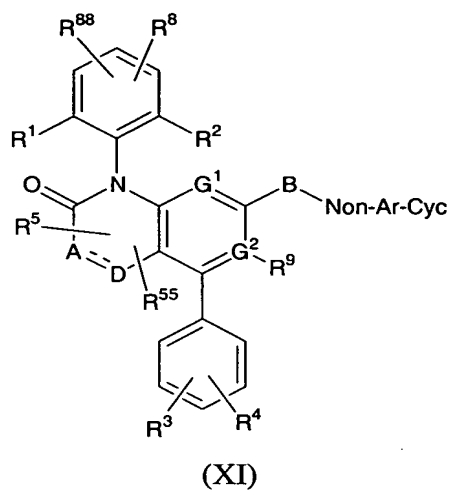
13. (new) The method of Claim 12 wherein the disease is Alzheimer's disease.

14. (new) The method of Claim 12 wherein the disease is mild cognitive impairment.

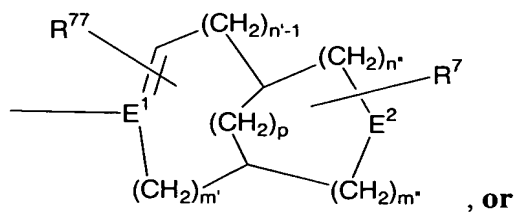
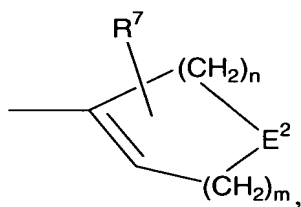
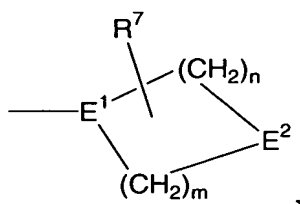
15. (new) The method of Claim 14 wherein the patient possesses one or more risk factors for developing Alzheimer's disease selected from: a family history of the disease; a genetic predisposition to the disease; elevated serum cholesterol; adult-onset diabetes mellitus; elevated baseline hippocampal volume; elevated cerebrospinal fluid levels of total tau; elevated cerebrospinal fluid levels of phospho-tau; and lowered cerebrospinal fluid levels of A β (1-42).

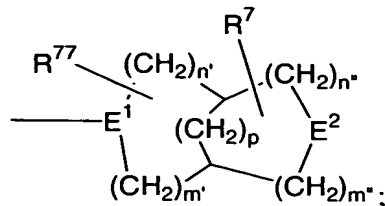
16. (new) The method of Claim 11 wherein the growth hormone secretagogue is N-[1(R)-[(1,2-dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethoxy)ethyl]-2-amino-2-methylpropanamide, or pharmaceutically acceptable salt thereof.

17. (new) The method of Claim 11 wherein the p38 kinase inhibitor is a compound of formula XI:



or pharmaceutically acceptable salts thereof, wherein
Non-Ar-Cyc is





A is N, O, NH, CH₂, or CH;

B is -C₁₋₆alkyl-, -C₀₋₃alkyl-O-C₀₋₃alkyl-, -C₀₋₃alkyl-NH-C₀₋₃alkyl-, -C₀₋₃alkyl-NH-C₃₋₇cycloalkyl-, -C₀₋₃alkyl-N(C₀₋₃alkyl)-C(O)-C₀₋₃alkyl-, -C₀₋₃alkyl-NH-SO₂-C₀₋₃alkyl-, -C₀₋₃alkyl-, -C₀₋₃alkyl-S-C₀₋₃alkyl-, -C₀₋₃alkyl-SO₂-C₀₋₃alkyl-, -C₀₋₃alkyl-PH-C₀₋₃alkyl-, -C₀₋₃alkyl-C(O)-C₀₋₃alkyl, or a direct bond;

D is CH, CH₂, N, or NH; optionally A and D are bridged by -C₁₋₄alkyl- to form a fused bicyclo ring with A and D at the bicyclo cusps;

E¹ is CH, N, or CR⁶; or B and E¹ form -CH=C<;

E² is CH₂, CHR, C(OH)R NH, NR, O, S, -S(O)-, or -S(O)₂-;

G¹ is N, CH, or C(C₁₋₃alkyl);

G² is N, CH, or C(C₁₋₃alkyl);

R, R⁷ and R⁷⁷ each independently is hydrogen, C₁₋₆alkyl- group, C₂₋₆alkenyl- group, C₄₋₆cycloalkyl-C₀₋₆alkyl- group, N(C₀₋₄alkyl)(C₀₋₄alkyl)-C₁₋₄alkyl-N(C₀₋₄alkyl)- group, -N(C₀₋₄alkyl)(C₀₋₄alkyl) group, C₁₋₃alkyl-CO-C₀₋₄alkyl- group, C₀₋₆alkyl-O-C(O)-C₀₋₄alkyl- group, C₀₋₆alkyl-C(O)-O-C₀₋₄alkyl- group, N(C₀₋₄alkyl)(C₀₋₄alkyl)-(C₀₋₄alkyl)C(O)(C₀₋₄alkyl)- group, phenyl-C₀₋₄alkyl- group, pyridyl-C₀₋₄alkyl- group, pyrimidinyl-C₀₋₄alkyl- group, pyrazinyl-C₀₋₄alkyl- group, thiophenyl-C₀₋₄alkyl- group, pyrazolyl-C₀₋₄alkyl- group, imidazolyl-C₀₋₄alkyl- group, triazolyl-C₀₋₄alkyl- group, azetidinyl-C₀₋₄alkyl- group, pyrrolidinyl-C₀₋₄alkyl- group, isoquinolinyl-C₀₋₄alkyl- group, indanyl-C₀₋₄alkyl- group, benzothiazolyl-C₀₋₄alkyl- group, any of the groups optionally substituted with 1-6 substituents, each substituent independently being -OH, -N(C₀₋₄alkyl)(C₀₋₄alkyl), C₁₋₄alkyl, C₁₋₆alkoxyl, C₁₋₆alkyl-CO-C₀₋₄alkyl-, pyrrolidinyl-C₀₋₄alkyl-, or halogen;

or R⁷ together with a bond from an absent ring hydrogen is =O;

n' + n'' = n;

m' + m'' = m;

n is 1, 2, 3, or 4;

m is 0, 1, 2, 3, or 4;

n+m is 2, 3, 4, 5, or 6;

p is 0, 1, 2, or 3;

R¹, R², R³, R⁴, and R⁶ are each independently halogen, C₀₋₄alkyl, -C(O)-O(C₀₋₄alkyl), or -C(O)-N(C₀₋₄alkyl)(C₀₋₄alkyl);

R⁵ and R⁵⁵ independently is H, CH₃, CH₂CH₃, or absent;

R⁸⁸ and R⁸ each is independently -CN, -C₀₋₄alkyl, -C(O)-N(C₀₋₄alkyl)(C₀₋₄alkyl), -C(O)-O-C₀₋₄alkyl or 1,3-dioxolan-2-yl-C₀₋₄alkyl-;

R⁹ is -C₀₋₄alkyl, or absent; and

any alkyl is optionally substituted with 1-6 independent halogen or -OH.

18. (new) A pharmaceutical composition comprising a growth hormone secretagogue or a pharmaceutically acceptable salt thereof, a p38 kinase inhibitor or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.